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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 01/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/658,991	SHABSIGH, RIDWAN	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-11* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/9/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *NOTICE TO COMPLY*.

DETAILED ACTION

Applicant's response of 10/14/05 is entered.

Claims 9-11 are presently pending.

Election/Restriction

Applicant's election with traverse of Group I, Claims 9-11, in the reply filed on 10/14/05 is acknowledged. The traversal is on the ground(s) that Applicant avers that there would be no serious burden on the Examiner to search and examine the two inventions together. This is not found persuasive because there would be a serious burden on the Examiner. To wit, these inventions are classified in separate classifications, and further, searching for either of these inventions would not necessarily bring up relevant art for the other, and further the considerations for each of the administration steps, and each of the genital areas requires distinct search and examination considerations. Such argument has been made in the Restriction of 9/9/05, pp. 2-3.

The requirement is still deemed proper and is therefore made FINAL.

Claim 11 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/14/04.

Therefore, Claims 9-10 are presently considered.

Specification

Applicant's specification is objected to for not containing the present status of parent Application No. 09/234,591, which issued as U.S. Patent No. 6,706,682. Applicant is required to update the status of the Application in the first paragraph of the specification.

The abstract of the disclosure is objected to because the abstract contains over 150 words. Correction is required. See MPEP § 608.01(b).

Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Specifically the application fails to comply with CFR 1.821(d), which states:

(d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

The specification discloses nucleotide sequences in on pages 17 (two sequences) and 18 (two sequences). However, these sequences are not identified by sequence identifiers, nor has Applicant submitted a sequence listing.

For compliance with sequence rules, it is necessary to include the sequence in the "Sequence Listing" and identify them with SEQ ID NO. In general, any sequence that is disclosed and/or claimed as a sequence, i.e., as a string of particular bases or amino acids, and that otherwise meets the criteria of 37 CFR 1.821(a), must be set forth in the "Sequence Listing." (see MPEP 2422.03).

For the response to this office action to be complete, Applicants are required to comply with the Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Information Disclosure Statement

The listing of references in the specification (pages 30-37) is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

An information disclosure statement (IDS) was submitted on 9/9/03. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. The references have been obtained from the parent Application; however, the reference to Burchardt, et al. from the Database Treemblerel has been crossed out because such lacks a date for the reference and accession number. Although Burchardt has been considered, due to the absence of a proper citation, such citation is crossed out to remove such reference from the face of any patent that may issue from this Application.

Claim Objections

Claim 10 is objected to because of the following informalities: Claim 10 recites the limitation "the nucleic acid comprises a vector". As such, the claim is interpreted to mean that the vector is any nucleic acid, and therefore excludes viral vectors. On the other hand, if Applicant means to claim more than simply such embodiments by the claim terminology (it is noted that page 14 of the specification defines vectors to include viral vectors), Applicant should amend accordingly; however, the objection will be withdrawn if Applicant provides appropriate argument.

Claim Rejections - 35 USC § 112 - Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-10 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Law

In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by Applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Such a determination is not a simple

factual consideration, but is a conclusion reached by weighing at least eight factors as set forth in In re Wands, 858 F.2d at 737, 8 USPQ.2d at 1404. Such factors are:

(1) The breadth of the claims;

(2) The nature of the invention;

(3) The state of the art;

(4) The level of one of ordinary skill in the art;

(5) The level of predictability in the art;

(6) The amount of direction and guidance provided by Applicant;

(7) The existence of working examples; and

(8) The quantity of experimentation needed to make and/or use the invention.

These factors will be analyzed, in turn, to demonstrate that one of ordinary skill in the art at the time of invention (hereinafter the "Artisan") would have had to perform "undue experimentation" to make and/or use the invention within its full scope, and that, therefore, Applicant's claims are not enabled to their full-claimed scope. In other words, in order to reasonably predict the working embodiments embraced by the full scope of Applicant's claims, the Artisan would have had to perform such extensive experimentation as to amount to inventing Applicant's claimed subject matter himself/herself.

As will be shown below, through the Wands factors, the Artisan would have to perform undue experimentation to reasonably predict the working embodiments embraced by Applicant's claims, which necessarily demonstrates a lack of enablement.

The Breadth of the Claims

Applicant's Claims 9-10 encompass a method for increasing or maintaining the blood supply in the penis of any subject, under any conditions, which comprises introducing any nucleic acid comprising any gene encoding any VEGF (which the Examiner interprets to mean any sequence encoding VEGF, operably linked to all the requisite expression control elements for its expression), into any suitable cell in the subject's penis, under any conditions permitting the expression of any VEGF in the cell, so as to thereby increase or maintain the blood supply in the subject's penis. Dependent claim 10 limits the nucleic acid to comprising a vector, which indirectly means that the nucleic acid is naked, and not encapsulated in any viral particle or liposome, etc.

Moreover, in light of Applicant's specification, it is clear that Applicant is not simply claiming increases in blood supply and maintaining the blood supply to the penis, in any subject, but the only reason for performing the methods, instead, is to treat erectile dysfunction and also specifically to treat it in humans (e.g., SPECIFICATION, pp. 1-4), and hence, Applicant's claims are required to be enabled for such treatment.

Such claims are broad, for increasing the blood supply in any subject penis, for maintaining the blood supply in any subject penis, for any nucleic acid, for any gene (which means any promoter and other expression sequences), for conditions permitting any VEGF to be expressed, even if its not the one transformed into the cells, for any method of administration, for VEGF expression without secretion, for any subject, and for any non-expression vector. The breadth of these aspects is so large as to require quite a bit of information for the Artisan to reasonably predict the working embodiments encompassed, without which the Artisan would have to perform undue experimentation. Such is now demonstrated below.

It is further stressed, in order to maintain a clear record, that Examiner has considered the Art and determined that VEGF forms are well known in the Art for many species and therefore, Applicant does not face a lack of enablement for the various forms of VEGF itself, but for the other elements in the claims.

The Nature of the Invention

Applicant's invention is in the nature of gene therapy. Despite much research over the last decade, however, gene therapy remains an art that is generally non-enabling of new inventions.

With regard to gene therapy, while progress has been made in recent years for gene transfer *in vivo*, vector targeting to desired tissues *in vivo* continues to be a difficulty as supported by numerous teachings available in the art. For example, Deonarain (1998) Expert Opin. Ther. Pat., 8: 53-69, indicates that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequeate levels for a long enough period of time" (p. 53, first paragraph). Deonarain reviews new techniques under experimentation in the art which show promise but states that such techniques are even less efficient than viral gene delivery (p. 65, CONCLUSION). Verma (1997) Nature, 389: 239-242, reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (p. 240, sentence bridging columns 2 and 3). Verma states that "The Achilles heel of gene therapy is gene delivery and this is the aspect we will concentrate on

here. Thus far, the problem has been an inability to deliver genes efficiently and to obtain sustained expression ... The use of viruses (viral vectors) is a powerful technique, because many of them have evolved a specific machinery to deliver DNA to cells. However, humans have an immune system to fight off the virus, and our attempts to deliver genes in viral vectors have been confronted by these host responses (e.g., p. 239, col. 3).

Further, Eck et al. (1996) Goodman & Gilman's The Pharmacological Basis of Therapeutics, McGraw-Hill, New York, NY., pp. 77-101, states that the fate of the DNA vector itself (volume of distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, and the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced, are all important factors for a successful gene therapy (e.g., bridging pp. 81-82). In addition, Gorecki (2001) Expert Opin. Emerging Drugs 6(2): 187-98) reports that "the choice of vectors and delivery routes depends on the nature of the target cells and the required levels and stability of expression" for gene therapy, and obstacles to gene therapy *in vivo* include "the development of effective clinical products" and "the low levels and stability of expression and immune responses to vectors and/or gene products" (e.g., ABSTRACT).

Therefore, in reviewing the general nature of gene therapy, it is clear that for the Artisan to reasonably predict that any particular gene therapy would be efficacious, enough information is required to reasonably predict that, for any particular gene therapy, through any particular

route of administration, that enough of the relevant tissue(s) will be transformed by the vector, express enough stable and functional mRNA (requiring proper expression control elements), and protein therefrom (requiring proper expression control elements), which protein will be trafficked to the site of action in large enough amounts (requiring proper protein signals), and for a long enough period of time to effect treatment. Moreover, such time frames are similarly suspect by the Artisan due to the possibility of immune reactions actually destroying any transformed cells before therapy could be effected.

Moreover, with regard to Applicant's claim to any vector, Applicant's claim necessarily comprises the use of non-expression vectors (SPECIFICATION, p. 14, first 3 full paragraphs). However, if such vector was not an expression vector, no VEGF would be expressed, and hence, the method could not be effected.

Lastly, with regard to conditions permitting the expression of any VEGF, such conditions much permit the expression of the VEGF which is being transferred by the nucleic acid, into the cell, otherwise, the method makes no sense, as Applicant has provided no methods for increasing the endogenously-encoded VEGFs, and the Art does not describe how to induce such conditions.

Therefore, the Artisan would not be able to reasonably predict the working embodiments embraced by Applicant's claimed invention.

The State of the Prior Art

The State of the Prior Art with respect to gene therapy VEGF in angiogenesis for erectile dysfunction (ED) reflects the same aspects as delineated in the nature of the invention. To wit, Bivalacqua, et al. (2001) J. Andrology, 22(2): 183-190, provides a review of the potential of gene therapy to effect treatment of erectile dysfunction. Bivalacqua first points to the various possible

causes of ED, which include psychological, arteriosclerosis, hypertension, diabetes, Peyronie disease, renal disease, pelvic trauma, and nerve damage (p. 183, col. 1, paragraph 2). From this, the Artisan would necessarily recognize that VEGF expression, which is generally recognized to be involved in angiogenesis, would not cure those causes of erectile dysfunction which do not involve problems with blood supply (e.g., psychological, diabetic (due to NOS, not vascularization, p. 187, col. 2, paragraph 1), and neurological disorders). Such is further emphasized in that Bivalacqua states that such erectile function depends on an intact central and peripheral nervous system and a stable hormonal status (p. 183, col. 2, paragraph 2). Moreover, erectile function involves three synergistic and simultaneous processes: (1) neurologically mediated increase in penile arterial inflow; (2) relaxation of the cavernosal smooth muscle (i.e., to obtain an influx of blood); and (3) restriction of venous outflow (Id.). Further, Bivalacqua makes clear that the corpora cavernosa is filled with vascularized sinuses, which fill with blood to cause the erection, and hence, it is therefore clear that these sinuses of the corpus cavernosa could theoretically benefit from increased vascularization (e.g., p. 184, col. 1, paragraph 2). However, the other portions of the penis, e.g., the corpus spongiosum, do not have any structure that would appear to benefit from increased vascularization (p. 183, col. 2, paragraph 2). Hence, the Artisan would recognize that, whatever the case, the tissue that would require vascularization is the corpus cavernosa, and would not reasonably predict that any other tissue could be treated.

Further, Bivalacqua also echos the various problems with vector, expression levels, and targeting expressed in the Nature of the Invention, demonstrating that the nature of the invention is relevant to Applicant's specifically claimed invention (e.g., pp. 184, col. 2, last paragraph). Further Bivalacqua discusses a variety of vectors, stating, "Each of these gene transfer vehicles

offers different gene transduction efficiencies and possesses distinct advantages and disadvantages. The ideal vector would be one that would allow efficient transduction and long-term stable transgene expression while demonstrating little or no adverse side effects, such as risk of infection, immunogenicity, or host-cell mutagenesis. However, despite numerous experimental attempts, the ideal vector has not yet been identified." (p. 185, paragraph 1). Further, with regard to humans, Bivalacqua recognizes that such therapy may lead to death before any therapeutic effect is attained, and the targeting of enough cells in the proper tissue is a problem (p. 187)Hence, clearly Bivalacqua recognizes all the same lack of reasonable predictability found in the nature of the invention applies to the claimed invention.

Moreover, while specific instances of NOS and hSlo transgene insertion by specific virus and plasmid vectors demonstrated improvement in specific instances in rats, these were administered directly to the corpus cavernosa, the encoded proteins were operatively linked to constitutive promoters, and the transgenes do not increase angiogenesis, but increase relaxation of the smooth muscle (pp. 188-189). However, Bivalacqua does not even discuss VEGF, and so the Artisan would not be able to reasonably predict that such therapy would work, as VEGF works through different mechanisms, and would necessarily require secretion of a sufficient amount of protein for a long enough period of time.

Lastly, Bivalacqua makes clear that such gene therapy is still being developed and requires much more research in order to enable it for the breadth of Applicant's claims (p. 189, last paragraph).

Hence, the Art, as reviewed by Bivalacqua does little to enable Applicant's invention.

Further, although little research has occurred with regard to Applicant's specifically claimed use of VEGF to treat erectile dysfunction, the research in VEGF indicates that the physiology of the body is such that it is not reasonably predictable that any particular tissue could be so-treated to increase/maintain vascularization, whether other factors may be required, and at what time VEGF may be required for treatment. Yancopoulos, et al. (2000) Nature, 407 : 242-48 reviews angiogenesis and the various growth factors required to obtain such angiogenesis. Yancopoulos makes clear at the outset that the action of VEGF in any particular tissue for effecting angiogenesis is required to act in concert, in both time and space, with a myriad of other factors, in order to obtain any angiogenic effect (p. 242, col. 1, paragraph 2). Hence, the Artisan would necessarily immediately recognize that the simple expression of VEGF in any particular tissue would not necessarily maintain or increase blood vessels in that tissue, as many other factors are required, in perfect harmony to obtain such effects. In fact, Yancopoulos regards the use of single growth factors in such methods to appear today to be "somewhat naïve and even misguided" (p. 242, paragraph bridging). On the other hand, with this same knowledge, the Yancopoulos also notes that inhibiting vascular ingrowth may be somewhat more enabled in the art (Id.). Moreover, in mature networks, any specific network of vascular tissue may require destabilization before new networks may grow, but such destabilization may actually cause vascular regression (p. 242, col. 2, paragraph 2). Further VEGF alone is only predicted to form leaky, immature, and unstable vessels (p. 243, col. 1, paragraph 2). This is all complicated by the fact that the VEGFs interact with overlapping, but also distinct receptors on the cell surface, and hence, if any particular VEGF is used, it is not reasonably predictable that the correct balance of factors will act in concert to induce/maintain angiogenesis (p. 243,

paragraph bridging columns). Moreover, it is also clear that from this requirement to act on the cell surface that any gene must necessarily encode the protein with the correct signal for secretion, and simply expression in the cell, as claimed by Applicant would not be enabled, as it would not be secreted to interact with the proper receptors.

In conclusion, Yancopolous indicates that there exists much potential for angiogenic growth factors, yet much still needs to be assessed before reasonably predictable therapies can result (p. 247).

Hence, it is further clear from Yancopolous that exquisite control is required of the VEGF expression and secretion, both in time and in space, to obtain any relevant angiogenesis that could obtain a therapeutic effect, or to maintain angiogenic levels in the tissue. Hence, the Artisan would not reasonably predict, even if the various aspects of gene therapy were overcome that any particular gene therapy with any particular tissue treatment would effect erectile dysfunction. Further, as Yancopolous makes clear, the Artisan would not reasonably predict that simple expression of VEGF within a cell would produce any effect, as these VEGF proteins interact with cell surface receptors, and hence, require secretion to interact with such receptors.

With regard to the administration of any viral expression vector (Claim 10), which the Examiner has interpreted to mean naked viral genomes only, not whole viral vectors (see claim objection, above), it is clear that many viruses require the whole viral particle in order to actually transform a cell. For Example, HIV requires the viral particle, because it contains the reverse transcriptase required for production of the positive strand, as well as integration into the genome (Freed, et al. (2001) Fundamental Virology, 4th Ed., Lippincott, Williams, and Wilkins, Philadelphia, PA, p. 944, Figure 17). Further transfer of RNA vectors, if they are the positive

strand would be very transient, and even less likely to provide enough of an effect for a long enough period of time. Lastly, administration of double stranded RNAs would be predicted by the Artisan to activate the RNAi pathways, and not obtain any therapy at all, as the RNA would then be cleaved by dicers (Banerjee, et al. (2002) BioEssays, 24(2): 119-129, p. 126), thereby destroying the gene encoded.

Hence, in view of the Nature of the invention, and state of the prior art, the Artisan would recognize various areas that lack reasonable predictability, including whether enough tissue is transformed, expresses enough stable and functional mRNA, and protein therefrom, which is then secreted to the site of action, for a long enough period of time to effect treatment, all without experiencing immune reactions that would destroy the transformed cells before any therapy takes place. Further, with regard to non-expression vectors, the Artisan would predict such VEGF not to be expressed in these cases, and therefore no therapy would be effected. Also, with regard to conditions permitting any VEGF to be expressed, the Artisan could not reasonably predict such conditions, except for expression of a transgene. Still also, with regard to viral vectors, such vectors would necessarily require the whole viral particle, as these vectors generally require factors in the particle to effect therapy, and with regard to RNA administrations, the Artisan would not predict such to work, due to RNAi interference and absence of reverse transcriptase. Further, the Artisan would not reasonably predict that any vascularization could be obtained or maintained in any particular tissue, due to the complexity of the vascular system factors, and their requirement to act in concert in both time and space. Lastly, the Artisan recognized that in order to enable a wide breadth of species, any particular

treatment would necessarily have to be shown efficacious in more than one animal type, and under multiple conditions.

Therefore, for these reasons, and the reasons in the Nature of the Invention, the Artisan would not be able to reasonably predict the working embodiments embraced by Applicant's claimed invention.

The Level of One of Ordinary Skill in the Art at the Time of Invention

The level of one of ordinary skill in the art at the time of invention was advanced, being that of a person holding a Ph.D. or an M.D.; however, because of the immaturity of the art, and its unpredictability, as shown by the other factors, one of skill in the art at the time of invention by Applicant would not have been able to make and/or use the invention without undue experimentation.

The Level of Predictability in the Art

Because of the art, as shown above, does not disclose enough to reasonably predict the various aspects discussed above, the Artisan could not predict, in the absence of proof to the contrary, that such applications would efficacious in any therapeutic treatment in any animal.

Hence, absent a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled.

The Direction and Guidance Provided by Applicant

Applicant's specification broadly discusses erectile dysfunction and the possible involvement of VEGF in correcting erectile dysfunction by increasing angiogenesis (pp. 1-4), a

brief description of the drawings (pp. 5-10), definitions (pp. 11-12), and broad description providing various administrations of VEGF and/or genes encoding such (pp. 12-15).

However, such description is broad and exceedingly vague, such as to amount to absolutely no specific direction and guidance, much less that direction and guidance that would be required to overcome the various aspects lacking reasonable predictability in the Art, as discussed above.

Hence, Applicant's description is deemed not to contribute anything over the nature of the invention and state of the prior art.

The Existence of Working Examples

Applicant's examples consist of a characterization of the forms of VEGF transcripts that are expressed in corporal tissues of human and rat penis. Applicant concludes that from such characterization, the goal of gene therapy with VEGF is one step closer to completion (p. 29). However, as Applicant's own specification implies with such statement, such gene therapy is not enabled by their characterization. Hence, the Examples in the specification do nothing to overcome the lack of enablement in the Art and nature of the invention.

The Amount of Experimentation Required to Practice the Invention

In light of the various Wands factors above, it is clear that the Artisan would require, to practice the invention to its fully-claimed scope, experimentation to determine the vector types that could be used, the promoters that could be used, the methods of administration that could be used, the forms of nucleic acid that could be used, the animals that could be treated, the causes of erectile dysfunction that could be treated, the tissues of the penis that could be treated, and the timing and coordination of VEGF expression with the other factors to effect any particular

maintenance or increase in blood supply to effect erectile dysfunction. Moreover, the Artisan would have to experiment to determine those non-expression vectors that could be used, and whether any particular nucleic acid could be used.

Such Experimentation amounts to undue experimentation.

Conclusion

Due to the finding of undue experimentation, Applicant's claimed invention is not enabled.

Claims Free of the Prior Art

Claims 9-10 are free of the prior art of record.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert M. Kelly, Ph.D.
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DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

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